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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,241	07/18/2006	Robert Dean Dally	X16604M	8270
25885 7590 03/26/2010 ELI LILLY & COMPANY PATENT DIVISION P.O. BOX 6288 INDIANAPOLIS, IN 46206-6288				
EXAMINER COLEMAN, BRENDA LIBBY				
ART UNIT		PAPER NUMBER		
1624				
NOTIFICATION DATE		DELIVERY MODE		
03/26/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary

Application No.

10/597,241

Applicant(s)

DALLY ET AL.

Examiner

Brenda L. Coleman

Art Unit

1624

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 18-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 18-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-13 and 18-28 are pending in the application.

This action is in response to applicants' amendment dated December 22, 2009.

Response to Arguments

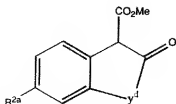
Applicants' arguments filed December 22, 2009 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 103, obviousness rejection labeled paragraph 2) in the last office action, the applicant's remarks have been fully considered but they are not persuasive. The applicants' stated that Grese discloses a genus of compounds which includes fluoro as a potential substituent. The applicants' further stated that when one reads beyond the broadest disclosure, Grese teaches a preference for hydroxy or derivatized hydroxy substituted compounds. The applicant raised several places in the reference where Grese described a preferred embodiment as set forth below (which have been labeled to better address each below):

- a. "Preferably, R^{1a} and R^{2a} are methoxy or a suitably protected hydroxyl, R^{3a} is -H, and X' is -O-." Column 9, lines 17-19.
- b. "Preferably R^{1a'} is -OH, R^{3a} is -H, X^d is OH, Y^d is CH₂CH₂, and R^{2a} is methoxy." Column 10, lines 57-58.
- c. "Preferably, R^{1a} and R^{2a} are suitably protected hydroxyls, R^{3a} is H, X is -O-, Y is -O- or -S-, and R⁶ is -C₆H₅." Column 12, lines 31-33.
- d. "In this embodiment of IIIc it is preferable that R^{1a} and R^{2a} are methoxy, R^{3a} is H, X is -N(COC₆H₅)- or -N(COC(CH₃)₄)-, Y is -O-, and R⁶ is preferably -C₂H₅." Column 12, lines 40-44.
- e. "In a preferred embodiment, in which R^{1a} and R^{2a} are t-butyldimethylsilyloxy or methoxy, R^{3a} is H, and G^a is -OSi(CH₃)₄" Column 14, lines 22-25.

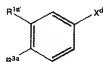
- f. "A preferred method for the deprotection of t-butylidimethylsilyl ethers, a preferred embodiment of R^{1a} and R^{2a} " Column 16, lines 18-20.
- g. "Preferred formula Ia compounds are those in which R¹ and R² each are methoxy, or R¹ and R² each are hydroxy, R³ is H, R⁴ is piperidinyl or pyrrolidinyl, X is -O-, Y is -S-, W is -CH₂-, and n is 1." Column 16, lines 26-29.
- h. "Preferred formula I compounds from this reaction are the same as those preferred formula I compounds described above " Column 16, lines 61-63.
- i. "Preferred formula VI compounds are those in which R^{1a} and R^{2a} are each individually -H or methoxy, and R^{3a} is -H. Most preferred is the compound in which both R^{1a} and R^{2a} are methoxy." Column 19, lines 36-40.
- j. "For example, when R^{1a}, R^{2a}, and/or R^{3a} of a formula IIe compound are C₁-C₄ alkyl hydroxy protecting groups, such groups can be removed via standard dealkylation techniques to prepare an especially preferred compound of formula IIe. In the most preferred examples of formula II compounds R¹ and R² are each individually -H, -OH, or methoxy, Y is -CH=CH-, B is -CH₂-, n is 1, W is -CH₂-, and R⁴ is 1-piperidinyl or 1-pyrrolidinyl. An alternative method involves the formation of preferred compounds of formula I or II by replacing the R¹, R², and/or R³ hydroxy groups of a formula I or formula II compound with methoxy." Column 21, lines 47-58.
- k. "Other preferred compounds of formula I or II are prepared by replacing the newly formed R¹, R² and/or R³ hydroxy groups of a formula I or formula II compound with a moiety of the formula -O-CO-(C₁-C₆ alkyl), or -O-SO₂-(C₄-C₆ alkyl) "Column 21, lines 62- 66.

One skilled in the art would know that in a reaction of a compound which contains multiple hydroxyl groups that it is necessary to protect the hydroxyl groups where the reaction should not occur. In the preferred embodiments pointed out by the applicant the protected hydroxys are necessary to prevent reaction at those sites. The reaction of the intermediates of formula Vb (preferred embodiment a); the tetralone or



indanone of the formula

is condensed with an appropriately



substituted phenol or thiophenol

(preferred embodiment b); the

intermediate of formula IIIc (preferred embodiment c and d); the intermediate of formula Ic (preferred embodiment e); the preferred method for the de-protection of t-butyldimethylsilylethers (preferred embodiment f); the intermediate of formula VI (preferred embodiment i); the intermediate of formula IIe (preferred embodiment j); the process of converting the hydroxyl substituted compounds of formula I and II to the moiety of the formula -O-CO-(C₁-C₆ alkyl) or -O-SO₂(C₁-C₆ alkyl) (preferred embodiment k), etc.

Compounds of the instant invention are within the scope of Grese's formulae I, Ia and Ib and therefore any preferred embodiments with respect to any other formula is not on point. The applicants' attention is drawn to a few other preferred embodiments which are directed to the compounds of formula Ib and formula I, i.e. column 13, lines 5-27, the compounds of formula Ib wherein R^{1a}, R^{2a} and R^{3a} are each independently -H, -O(C₁-C₄ alkyl), -Cl, -F or a suitably protected hydroxyl and column 16, lines 24-25, pharmaceutically active compounds of formula I in which R¹, R² and R³ each are hydrogen, hydroxyl, C₁-C₄ alkoxy, chloro, or **fluoro**. The closest compound of Grese is

Example 11b which differs from the compounds of the instant invention by the 8-hydroxy versus an 8-fluoro. In view of the preferred embodiment of formula I where R¹ is only ten possible moieties and thus one of ordinary skill in the art would be motivated to select a fluoro moiety for the variable R¹ as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the preferred embodiments outlined above.

Claims 1-13 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over GRESE et al., U.S. Patent No. 6,133,288; 6,004,971; and 5,726,186, for reasons of record and stated above.

2. With regards to the nonstatutory obviousness-type double patenting rejection as being unpatentable over claims 1-11, 13, 18-26 and 28 of U.S. Patent No. 5,726,186 labeled paragraph 3) in the last office action, the applicants' stated that based on the applicant's arguments set forth above with respect to the rejection under 35 U.S.C. § 103(a) for being unpatentable over Grese et al., 5,726,186 the applicants reiterate the same arguments set forth therein and respectfully submit that the claimed compounds are not prima facie obvious over U.S. 5,726,186. However as stated above the compounds are prima facie obvious over Grese 5,726,186 and thus the rejection of claims 1-11, 13, 18-26 and 28 are herein maintained.

Claims 1-11, 13, 18-26 and 28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,726,186. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the compounds of formula I and II where R¹ is F, for reasons of record and stated above.

3. With regards to the nonstatutory obviousness-type double patenting rejection as being unpatentable over claims 1-5 and 18-20 of U.S. Patent No. 6,004,971 labeled paragraph 4) in the last office action, the applicants' stated that based on the applicant's arguments set forth above with respect to the rejection under 35 U.S.C. § 103(a) for being unpatentable over Grese et al., 6,004,971 the applicants reiterate the same arguments set forth therein and respectfully submit that the claimed compounds are not prima facie obvious over U.S. 6,004,971. However as stated above the compounds are prima facie obvious over Grese 6,004,971 and thus the rejection of claims 1-5 and 18-20 are herein maintained.

Claims 1-5 and 18-20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,004,971. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds of formula I and II where R¹ is F.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624